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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,660	12/22/2000	Markus Pompejus	BGI-121CP2	1463

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/746,660	POMPEJUS ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-27 and 41-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Non-Compliance.*

DETAILED ACTION

This Office action is in response to the communications filed 6-24-02 and 9-18-03.

Claims 1-47 are pending in the instant application.

Restriction/Election

Claims1-27, 41-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the restriction election filed 12-31-02.

Applicant's election without traverse of Group III in the restriction election filed 12-31-02 is acknowledged.

Applicant's election with traverse of SEQ ID NO: 1 in the restriction election filed 9-18-03 is acknowledged. The traversal is on the ground(s) that a reasonable number of sequences examined should include up to ten sequences per invention in order to save cost and time for Applicants. This is not found persuasive because the expanding data bases required to adequately search each of the sequences claimed makes the search of more than one sequence an unreasonable burden to the examiner and to the searching facilities that are required for an adequate search. The MPEP suggests guidelines that may include up to ten sequences, but these guidelines were suggestions, not guarantees for Applicant. Furthermore, these suggested guidelines did not anticipate the ever-expanding data bases and the increasing burden that

accompanies such expanding data bases. Searching more than one of the sequences claimed would create an unreasonable burden, therefore, the restriction requirement is maintained.

The requirement is still deemed proper and is therefore made FINAL.

Priority Information

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on July 8, 1999. It is noted, however, that applicant has not filed a certified copy of the provisional application as required by 35 U.S.C. 119(b).

Objection to the Specification – Possible Sequence Non-Compliance

On page 79, line 22, a space has been left blank that refers to a vector pB. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **On page 79 of the specification, line 22, a space has been left blank that refers to a vector pB, presumably regarding its accompanying SEQ ID NO. Please provide the appropriate sequence and SEQ ID NO for this vector if appropriate, or otherwise correct the omission appropriately.** See the accompanying Notice to Comply.

Claim Objections

Claims 28, 33, 35, 36, 37, 38 are objected to because of the following informalities: Claims 28, 33, 36-38 depend from non-elected claims. Claim 35, line 9, and claim 37, line 5, both refer to Tables in the specification. If possible, please avoid reference to Tables or Figures in the specification in the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 30 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 recites the limitation "said culture" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 35 depends from claim 27, which is a composition claim (perhaps replacing "27" with –28— in line 1 would be remedial).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to methods for producing a fine chemical, including an amino acid, in a cell, and which cell has been altered with one or more metabolic pathway nucleic acid molecules, including SEQ ID NO: 1, or a nucleic acid encoding SEQ ID NO: 2, their allelic variants or 50% homologues. The specification and claims do not describe elements which are essential to various functions of the claimed invention, including those essential to the genera comprising *fine chemicals*, *metabolic pathway nucleic acid molecules*, *allelic variants or homologues* of SEQ ID NO: 1, or nucleic acid encoding SEQ ID NO: 2. The specification and claims do not indicate what distinguishing attributes are concisely shared by the members of these very broad genera. The disclosure does not clarify what the common attributes are encompassed by fine chemicals, metabolic pathway nucleic acid molecules, allelic variants and homologues of the nucleic acid sequences claimed. The scope of the claims includes numerous structural variants, and the genera are highly variant because a significant number of structural differences between members of a given genus is permitted. Concise structural features that could distinguish structures or compounds within a genus from others are missing from the disclosure. No common structural attributes identify the members of the genus comprising fine chemicals, metabolic pathway

nucleic acid molecules, allelic variants or homologues of SEQ ID NO: 1 or nucleic acids encoding SEQ ID NO: 2. And the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. The specification fails to teach or adequately describe a representative number of species in each genus such that the common attributes or characteristics concisely identifying members of each proposed genus are exemplified. And because each genus is highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the various genera claimed. Thus, applicant was not possession of the claimed genera.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for altering amino acid metabolism in an isolated host cell (i.e. reduction of lysine, accumulation of homocysteine and methionine) in vitro following transformation of the cell with a nucleic acid comprising SEQ ID NO: 1, encoding SEQ ID NO: 2, does not reasonably provide enablement for a method of producing fine chemicals comprising the transformation of an appropriate host cell with SEQ ID NO: 1, encoding SEQ ID NO: 2, or any allelic variant thereof, or any nucleic acid that is 50% homologous to SEQ ID NO: 1 or 50% homologous to a nucleic acid encoding SEQ ID NO: 2. The specification does not enable any person skilled in the art

to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a method of producing fine chemicals comprising the stable tranformation of an appropriate host cell with SEQ ID NO: 1, encoding SEQ ID NO: 2, or any allelic variant thereof, or any nucleic acid that is 50% homologous to SEQ ID NO: 1 or 50% homologous to a nucleic acid encoding SEQ ID NO: 2.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of producing fine chemicals comprising transforming cells with SEQ ID NO: 1, encoding SEQ ID NO: 2. Applicants have not provided guidance in the specification toward a method of altering amino acid metabolism comprising the administration of any allelic variant of SEQ ID NO: 1, nor of any 50% homologue of SEQ ID NO: 1, or of any nucleic acid encoding SEQ ID NO: 2. The specification teaches a reduction in lysine production, and an accumulation in homocysteine and methionine in host cells that are lysine over-expressors following transformation of these cells with SEQ ID NO: 1 in vitro. The specification fails to teach a method of producing all fine chemicals comprising the transformation of host cells with SEQ ID NO: 1. The specification also fails to teach a method of altering amino acid metabolism or producing any fine chemicals comprising the transformation of host cells

with allelic variants or 50% homologues of SEQ ID NO: 1, encoding SEQ ID NO: 2. One skilled in the art would not accept on its face the examples given in the specification of the reduction in lysine production, and an accompanying accumulation in homocysteine and methionine in host cells that are lysine over-expressors following transformation of these cells with SEQ ID NO: 1 in vitro, as being correlative or representative of the ability to produce all fine chemicals in view of the lack of guidance in the specification and unpredictability associated with the ability to predict the production of all fine chemicals comprising the transformation of host cells with SEQ ID NO: 1, and the unpredictability of functional allelic variants and function homologues of SEQ ID NO: 1 or encoding SEQ ID NO: 2, and further whereby all fine chemicals are produced. The specification as filed fails to provide any particular guidance which resolves the unpredictability in the art associated with producing all fine chemicals following the transformation of the instant nucleic acids claimed, and regarding any allelic variants and as low as 50% homology with SEQ ID NO: 1, or encoding SEQ ID NO: 2.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to a method of producing fine chemicals comprising the stable transformation of an appropriate host cell with SEQ ID NO: 1, encoding SEQ ID NO: 2, or any allelic variant thereof, or any nucleic acid that is 50% homologous to SEQ ID NO: 1 or 50% homologous to a nucleic acid encoding SEQ ID NO: 2. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of host cell transformation

of SEQ ID NO: 1 or any nucleic acid encoding SEQ ID NO: 2, its functional allelic variants and its functional homologues whereby 50% of the sequence is homologous, and further whereby any fine chemical is produced. Since the specification fails to provide any particular guidance for the production of all fine chemicals comprising the transformation of a nucleic acid encoding SEQ ID NO: 2, its allelic variants or 50% homologues, and since determination of these factors is highly unpredictable, it would require undue experimentation to practice the invention over the broad scope claimed.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose

telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

JZ
December 14, 2003